

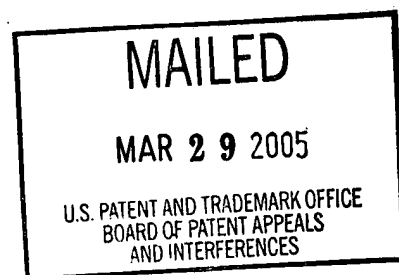
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte MICHAEL D. EDGE, DAN POLLOCK,
YANN ECHELARD, HARRY M. MEADE, and SUSANNA M. RYBAK

Appeal No. 2004-2207
Application No. 09/398,610

ON BRIEF¹



Before ELLIS, ADAMS, and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-8, 10-14 and 16-35, which are all the claims pending in the application. However, notwithstanding the examiner's rejection of all pending claims (claims 1-8, 10-14 and 16-35), the examiner has limited the scope of her review of the record to the elected species of the second member of the claimed fusion protein – angiogenin. Answer, page 4. According to the examiner (id.), "[c]laims 8 and 30 are limited to the elected subject matter of a fusion protein comprising angiogenin. ... All pending claims, including generic

¹ Appellants waived their request for oral hearing. Paper received February 25, 2005. Accordingly, we considered this appeal on Brief.

claims 1-7, 10-14, 16-29, and 31-35, have been examined only to the extent that they read on the elected subject matter." Accordingly, we take no position with respect to the patentability of the non-elected species. See Ex parte Ohsaka, 2 USPQ2d 1460, 1461 (Bd. Pat. App. & Int. 1987).

Claims 16, 24 and 30 are illustrative of the subject matter on appeal and are reproduced below:

16. A non-human transgenic mammal which includes a transgene that encodes a fusion protein, the transgene comprising: a mammary epithelial specific promoter, a nucleotide sequence which encodes a signal sequence which can direct the secretion of the fusion protein, and one or more nucleotide sequences encoding the fusion protein, wherein the fusion protein includes a first member and a second member, the second member is an enzyme produced in the milk of a transgenic mammal in biologically active form, and the fusion protein is produced in the milk of the transgenic mammal at a concentration of at least about 0.1 mg/ml.
24. The transgenic mammal of claim 16, wherein the first member of the fusion protein is an immunoglobulin subunit.
30. The transgenic mammal of claim 16, wherein the second member of the fusion protein is angiogenin.

The references relied upon by the examiner are:

Hyttinen et al. (Hyttinen)	5,959,171	Sept. 28, 1999
Rybak et al. (Rybak), "Humanization of immunotoxins," <u>Proc. Natl. Acad. Sci. USA</u> , Vol. 89, pp. 3165-3169 (1992)		

GROUND OF REJECTION

Claims 1-8, 10-14, and 16-35 stand rejected under 35 U.S.C. § 103 as being unpatentable over Hyttinen in view of Rybak.

We affirm.

CLAIM GROUPING

The claims stand or fall together. Brief, page 7. Since all claims stand or fall together, we limit our discussion to representative independent claim 16.

Claims 1-8, 10-14, and 17-35 will stand or fall together with claim 16. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

DISCUSSION

As we understand it, claim 16 is drawn to a non-human transgenic mammal that contains a fusion protein transgene, and produces the fusion protein in milk of the transgenic mammal at a concentration of at least about 0.1 mg/ml. The claimed transgene comprises a:

1. mammary epithelial specific promoter,
2. nucleotide sequence which encodes a signal sequence which can direct the secretion of the fusion protein,
3. one or more nucleotide sequences encoding the fusion protein which includes a
 - a. first member, e.g., an immunoglobulin subunit, and
 - b. second member – angiogenin, which is produced in the milk of a transgenic mammal in a biologically active form.²

According to the examiner (Answer, page 5), Hyttinen “teaches vectors encoding a fusion protein which comprises a biologically active protein operatively linked to regulatory elements needed for high level mammary gland specific expression ... a DNA sequence encoding a signal sequence needed for

² According to appellants (Brief, page 11), “the claims recite the term ‘biologically’ active form, and this expressly incorporates this important element and limitation into the claimed molecular construct of the invention....” However, as discussed infra, appellants, fail to identify any portion of their specification that defines the term “biologically active.”

secretion and maturation of the fusion protein (Hyttinen et al., column 3, particularly lines 15-54).” In addition, the examiner finds (id.), Hyttinen “teaches transgenic animals ... made using said vectors, and methods of making a bioactive fusion protein comprising collecting milk from a transgenic mammal which expresses protein in its milk, and isolating the recombinant fusion protein from the milk (Hyttinen et al., column 3, lines 15-61, and column 5, lines [sic]).” Regarding the requirement in appellants’ claim that the enzyme produced in the transgenic mammals milk be in a biologically active form, the examiner finds (Answer, bridging sentence, pages 5-6), Hyttinen states that, “[t]he biologically active protein shall be understood to cover any potent polypeptide that in its free form could cause adverse effects in the producing mammal. Such polypeptides are for example ... enzymes and the like’ (Hyttinen et al., column 4, lines 3-10).” In addition, the examiner finds (Answer, page 6), “in one exemplified embodiment, Hyttinen et al. teaches making and using a transgenic mammal which expresses a beta-lactoglobulin-hEPO fusion protein at concentrations of 0.2-1 mg/ml in the transgenic milk (Hyttinen et al., column 10, lines 30-35).”³

From the foregoing, the examiner concludes (id.), “Hyttinen establishes that at the time of filing, the state of the art of making transgenic mammals which secrete biologically active proteins in the milk was high, and that the prior art recognized the advantages of producing large quantities of biologically relevant,

³ According to the examiner (Answer, page 6), “hEPO is an enzyme.”

thereapeutic proteins in milk of transgenic animals.”⁴ The examiner recognizes, however, that Hyttinen does not teach “the production of a fusion protein comprising angiogenin.” Id. The examiner relies on Rybak to make up for this deficiency in Hyttinen.

According to the examiner (Answer, page 6), Rybak teaches “nucleic acid expression constructs which encode a secretable fusion protein comprising a single chain antibody against the human transferrin receptor and angiogenin (Rybak et al., abstract).” While the examiner recognizes (Answer, bridging sentence, page 6-7) that Rybak teach the expression of the fusion protein in mammalian cell lines in vitro, the examiner finds (Answer, page 7), “the skilled artisan would have been motivated to express the fusion protein taught by Rybak et al. using a mammalian bioreactor system in order to produce larger quantities of the human fusion protein as taught by Hyttinen....”

Based on this evidence, the examiner concludes (Answer, page 7),

it would have been prima facie obvious to the skilled artisan at the time of filing to express the fusion protein comprising angiogenin taught by Rybak et al. using the transgenic bioreactors taught by Hyttinen. Further, based on successful use of transgenic bioreactors in expressing large quantities of a variety of human proteins and enzyme containing fusion proteins as taught by Hyttinen et al., the skilled artisan would have had a reasonable expectation of success in expressing the fusion protein comprising the a [sic] single chain antibody against the transferrin receptor and angiogenin in the milk of a transgenic mammal according to the methods taught by Hyttinen et al.

⁴ We note that portions of the Answer refer to the production of proteins in milk of transgenic animals as a “mammalian bioreactor system.” See also Hyttinen, column 1, lines 18-32.

In response appellants present a number of arguments. We take each in turn.

I. The biological activity of Hyttinen's fusion proteins:

According to appellants (Brief, page 10), Hyttinen teaches away from the claimed invention by using a transgenic animal to produce inactive molecules, which are later available for activation. In this regard, appellants note (id.), Hyttinen, "disclose that there can be 'severe side effects' when 'producing potent polypeptides like growth factors, cytokines or enzymes' in the milk of transgenic mammals.... To solve such problems, Hyttinen et al. disclose producing such polypeptides as part of a fusion protein such that the polypeptide is produced in the milk of the animal in inactive form." According to appellants (id.), in contrast to the invention of claim 16, which is drawn to, inter alia, an enzyme fusion protein "produced in the milk of a transgenic mammal in biologically active form," Hyttinen "state that polypeptides (such as enzymes) are produced 'as fusion proteins that are less active than said biologically active polypeptide in its free form, or non-active....'"

The examiner recognizes (Answer, page 8), Hyttinen's enzyme fusion proteins are biologically less active than the free form of the enzyme. Nevertheless, the examiner finds (id.), "[w]hile the fusion proteins described by Hyttinen ... may not demonstrate 100% of the activity of the free wild type enzyme, a less active enzyme still equates to a 'biologically active' enzyme as required by ... [claim 16] as written." In this regard, the examiner finds (id.),

claim 16 does “not recite any specific level of activity, nor does the specification as filed define the phrase ‘biologically active form’ as meaning that the enzyme present in the form of a fusion protein has 100% of the enzymatic activity as the enzyme in its free form.”⁵

According to appellants (Brief, page 11), “unlike Hyttinen, the claimed first member does not reduce the activity of the second member of the fusion protein.” In response, the examiner finds (Answer, page 9), “the claims on appeal do not in fact contain any such limitation.” On reflection, we find that the examiner has the better argument.

“The name of the game is the claim.” In re Hiniker Co., 150 F.3d 1362, 47 USPQ2d 1523, 1529 (Fed. Cir. 1998). In considering the issues raised in this appeal, we point out that “analysis begins with a key legal question – what is the invention claimed?” since “claim interpretation ... will normally control the remainder of the decisional process.” Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1567, 1 USPQ2d 1593, 1596 (Fed. Cir.), cert. denied, 481 U.S. 1052 (1987). As discussed above, claim 16 is drawn, inter alia, to a non-human transgenic mammal that produces an enzyme fusion protein in the milk of the transgenic mammal in biologically active form. As the examiner points out, claim 16 does not place a limitation on the scope of this biological activity, nor does appellants’ specification. As the examiner explains (Answer, page 8), “[t]he phrase ‘biologically active form’ is very broad and reads on a fusion protein where the enzyme portion has any level of biological activity.” We agree. As

⁵ Appellants have not disputed this assertion.

discussed, infra, Hyttinen teaches a fusion protein expressed in the milk of a transgenic mammal that has biological activity.

In addition, Hyttinen discloses (column 2, lines 55-62), an objective of the invention “is to provide a fusion protein [(which may be an enzyme fusion protein)], which is less active than the biologically active polypeptide in free form....” Hyttinen accomplishes this by fusing the enzyme with another “peptide or amino acid that can be cleaved to release the desired biologically active polypeptide in its free native form.” Id. As set forth in the Manual of Patent Examining Procedure § 2111.03, “[t]he transitional term ‘comprising’, which is synonymous with ‘including,’ ‘containing,’ or ‘characterized by,’ is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.” Emphasis added. According to claim 16, “the fusion protein includes a first member and a second member....” As we understand the claim, the use of the term “includes” does not limit the scope of the fusion protein to just a first member and a second member. To the contrary, the term “includes” opens the claim to read on a fusion protein that comprises a first member, a second member, and another member that will, as taught by Hyttinen, reduce the activity of the enzyme component of the fusion protein.

For the foregoing reasons, we are not persuaded by appellants' argument.⁶

II. Hyttinen constitutes a failed experiment:

According to appellants (Brief, page 11), "mice used as an example of a productive 'bioreactor' in ... [Hyttinen], demonstrate very high hematocrit levels, when no active exogenous or transgenic erythropoietin was supposed to be in their systems due to the 'protections' provided by the Hytinnen [sic] invention." In this regard, appellants note (id.), "[t]he hematocrit levels that Hytinnen [sic] reports simply would not be seen [in the] absence of transgenically produced erythropoietin in their systems. ([S]ee, Example 3 (mouse line 115) as provided in Hytinnen [sic] et al., Figure 2, and claim 3)."

In response, the examiner finds (Answer, page 9),

The working example described by Hyttinen et al. in fact presents a fully successful example of their invention. The transgenic mice described in column 10 of Hyttinen express the beta-lactoglobulin-hEPO fusion protein in their milk at high concentrations (0.2-1 mg/ml) and are healthy (Hyttinen et al., column 10, lines 30-38). The fact that one of the mice had a slightly elevated hematocrit, while still considered healthy, simply proves that the fusion protein was in fact biologically active.

Upon review of the record, we find that the examiner has the better argument. A stated objective of Hyttinen "is to provide a process for the production and secretion of a biologically active polypeptide as a fusion protein

⁶ We recognize appellants' discussion bridging pages 13-14, and what appears to be a block quote extracted from an Office Action. Appellants however, fail to identify the source of this quote. In addition, the examiner finds (Answer, page 11), appellants' quoted text "does not come from the rejection of record which was first presented in the Office action mailed on 6/17/02 on pages 3-6, or any other communication from the [e]xaminer mailed to the applicants." Accordingly, we are not persuaded by appellants' assertion.

into the milk of a mammal without causing to said mammal severe side effects....” Hytinen, column 2, lines 50-54. As the examiner points out, example 3 of Hytinen discloses (column 10, lines 35-38), “[t]he transgenic mice expressing the fusion protein are so far healthy and the hematocrits were within normal range except in line 115, in which the hematocrit was slightly elevated....” Accordingly, in contrast to appellants’ assertion, we agree with the examiner’s finding (Answer, page 9) “[t]he fact that one of the mice had a slightly elevated hematocrit, while still considered healthy, simply proves that the fusion protein was in fact biologically active.”

For the foregoing reasons, we are not persuaded by appellants’ argument.

III. Ryback is non-analogous art:

According to appellants (Brief, page 14),

The system of the invention is a transgenic living mammal, it is highly unlikely that anyone in the field of transgenics would look to a reference promoting the intracellular production and accumulation of toxins in transfectomas or related cell lines for guidance on how to allow or optimize the production of an active immunotoxin in a whole animal secretory expression system.... In this light Ryback et al., is simply non-analogous art incapable of supporting an obviousness rejection of the instant claims....

In this regard, appellants assert (Brief, page 16), “the Ryback reference is not only silent with regard to transgenic animals but rather focuses and provides teaching with regard only to simple expression in prokaryote expression vectors-essentially teaching away from the methods required to achieve success in the expression of immuno-fusion sequences in transgenic animals.”

"In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). See also In re Deminski, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986). According to the examiner (Answer, page 12), Rybak

teaches the production of a fusion protein comprising an immunoglobulin which recognizes transferrin and angiogenin in a mammalian tissue culture system in vivo. The fusion protein taught by Rybak et al. is identical to the preferred embodiment of appellant's [sic] invention as disclosed in the specification, and broadly claimed in the claims on appeal. Thus, Rybak et al. is clearly pertinent to the particular protein with which the appellant[s] is [sic] concerned and is further clearly in the appellant's [sic] field of endeavor.

As set forth in In re Clay, 966 F.2d 656, 659, 23 USPQ2d 1058, 1060-61 (Fed. Cir. 1992), "[a] reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem."

Here, as the examiner explains, Rybak teaches a fusion protein comprising an immunoglobulin and an angiogenin, which is one of the preferred embodiments of appellants' invention as disclosed in their specification. According to appellants' specification (e.g., page 4), "[i]n preferred embodiments, the transgenic fusion protein includes an immunoglobulin heavy chain or fragment thereof ... linked via a peptide linker or directly fused, to an enzyme. In preferred embodiments, the enzyme of the fusion protein is ... angiogenin."

According to Rybak (Abstract), "F(ab')₂-like antibody-enzyme fusions were prepared by linking the gene for human angiogenin to a chimeric anti-transferrin receptor heavy chain gene." See also Brief, page 14, wherein appellants recognize Rybak "discloses the production of a fusion protein consisting of an immunoglobulin heavy chain and angiogenin...."

Appellants' assertions to the contrary, we find Rybak to be analogous to the invention of claim 16. Accordingly, we are not persuaded by appellants' argument.⁷

IV. Ryback provides no reasonable expectation of success:

According to appellants (Brief, page 14), Rybak "discloses the production of a fusion protein consisting of an immunoglobulin heavy chain and angiogenin in a culture system. Rybak et al. disclose that this fusion protein is secreted into cell culture at extremely low levels." Thus, appellants conclude (Brief, page 15),

neither the Hyttinen et al. reference nor the Rybak et al. reference alone or in combination provide any indication of a likelihood of success in expressing reported poorly expressed protein in the milk of a transgenic mammal in which secretion is an essential step in recovering the fusion protein at levels as high as at least ... [about 0.1 mg/ml].

In response, the examiner finds (Answer, page 14),

[t]here is nothing alien or non-analogous about the production of a fusion protein in mammalian cells in vitro, particularly in light of the teachings of Hyttinen et al. which provides substantial motivation

⁷ We also recognize appellants' assertion (Brief, page 15), "[a]t best, the Ryback citation provides an E. coli platform for use in and with a variety of well known vectors including prokaryotes." However, as the examiner points out (Answer, page 13), "this is incorrect. Ryback does not teach the expression of the fusion protein in E. coli. The entire Ryback et al. reference teaches the production of the fusion protein in mammalian cells." Accordingly, we are not persuaded by appellants' argument.

for producing fusion protein in the milk of transgenic mammals rather than in mammalian tissue culture in order to produce substantially greater amounts of the desired fusion protein.

Further, the examiner finds (Answer, page 17), Hyttinen provides specific examples demonstrating the expression of a fusion protein in the milk of transgenic mammals at levels between 0.1-1mg/ml. Accordingly, the examiner finds (Answer, page 18), based on the combination of references relied upon, “the skilled artisan would have had a reasonable expectation of success in expressing the fusion protein taught by Rybak et al. in large amounts in milk using the transgenic bioreactor system taught by Hyttinen et al.” We remind appellants that obviousness does not require absolute predictability of success. For obviousness under §103, all that is required is a reasonable expectation of success. In re O’Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

For the foregoing reasons, we are not persuaded by appellants’ arguments.

V. No motivation to combine:

To be complete, while appellants mention the lack of a motivation to combine the references of record in their discussion of unexpected results, we will discuss these issues separately. According to appellants (Brief, page 20), “[t]he fact that Hyttinen ... disclose using mammals ‘which produce large quantities of milk and have long lactation periods,’ provides absolutely no

suggestion that the claimed fusion proteins, which were secreted so poorly in the cell culture, could be secreted at levels of 0.1 mg/ml in milk."

There is no doubt that a prima facie obviousness based on a combination of references requires that the prior art provide "a reason, suggestion, or motivation to lead an inventor to combine those references." Pro-Mold and Tool Co. v. Great Lakes Plastics Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996). We note, however, as set forth in In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999), citations omitted,

evidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. . . . The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular.

On this record, appellants recognize (Brief, page 14), Rybak teach "the production of a fusion protein consisting of an immunoglobulin heavy chain and angiogenin in a culture system." More specifically, Rybak teach a humanized immunotoxin, comprising an immunoglobulin heavy chain and angiogenin, which may be used to target tumor cells. See e.g., Rybak, page 3169, column 1, second full paragraph. According to Rybak (page 3169, column 2, last paragraph), "this paper demonstrates the acquired cytotoxic potential of a human RNase when it is linked to a chimeric antibody." However, as appellants point out (Brief, page 14), the Rybak fusion protein was expressed at extremely low levels in cell culture. According to the examiner (Answer, page 6), "Hyttinen establishes that at the time of filing, the state of the art of making transgenic

mammals which secrete biologically active proteins in the milk was high, and that the prior art recognized the advantages of producing large quantities of biologically relevant, therapeutic proteins in milk of transgenic animals.” The examiner also finds (Answer, page 6), Hyttinen “differs from the instant invention by not specifically teaching the production of a fusion protein comprising angiogenin.”

Therefore, as the examiner explains (Answer, page 7), given the successful use of transgenic animals in expressing large quantities of a variety of human proteins and enzyme-containing fusion proteins the skilled artisan would have been motivated to express Rybak’s humanized immunotoxin in transgenic animals as taught by Hyttinen. We agree.

Accordingly, we are not persuaded by appellants’ assertion that there is no motivation to combine the references of record.

VI. Long Felt Need

We agree with appellants (Brief, page 17), “[a] showing that an invention can satisfy a long felt need for a problem is relevant evidence of the non-obviousness and patentability of an invention.” In re Sernaker, 702 F.2d 989, 996, 217 USPQ 1, 7 (Fed. Cir. 1983) (“When objective evidence of nonobviousness is available it must be considered.”). In this regard, we

recognize appellants' reference to Frankel⁸ and Nagy⁹ which, according to appellants, "demonstrate the ongoing need for a production method of the type presented by the instant invention..."

However, as the examiner points out (Answer, page 15), "the papers filed on 10/23/03 did not contain any such references or abstracts. Therefore, the relevance of the teachings of Frankel et al. and Nagy et al. cannot be determined." Our review of the image file wrapper (IFW), also indicates that the references are not of record. Accordingly, we find no objective evidence of a long-felt need on this record.

We remind appellants, as did the examiner (Answer, page 15), "arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965)."

Accordingly, we are not persuaded by appellants' argument.

VII. Unexpected Results:

According to appellants (Brief, page 20),

The fact that Hyttinen ... disclose using mammals "which produce large quantities of milk and have long lactation periods," provides absolutely no suggestion that the claimed fusion proteins, which were secreted so poorly in the cell culture, could be secreted at levels of 0.1 mg/ml in milk. This was an unexpected result of the claimed invention.

⁸ Frankel et al. (Frankel), "Anthrax Fusion Protein Therapy of Cancer," Curr. Protein Pept. Sci., Vol. 3, No. 4, pp. 399-407 (2002).

⁹ Nagy et al. (Nagy), "Fully Human, HLA-DR-Specific Monoclonal Antibodies Efficiently Induce Programmed Death of Malignant Lymphoid Cells," Nat. Med., Vol. 8, No. 8, pp. 801-907 (2002).

We remind appellants, as set forth in In re Freeman, 474 F.2d 1318, 1324, 177 USPQ 139, 143 (CCPA 1973):

In order for a showing of “unexpected results” to be probative evidence of non-obviousness, it falls upon the applicant to at least establish: (1) that there actually is a difference between the results obtained through the claimed invention and those of the prior art; and (2) that the difference actually obtained would not have been expected by one skilled in the art at the time of the invention.

Appellants provide no evidence to support their assertion that the results obtained by the invention of claim 16 would have been unexpected.

Arguments of counsel cannot take the place of evidence on this record.

Schulze.

Further, we are not persuaded by appellants' assertion (Brief, page 20) that Hyttinen's example relates to the use of a native milk protein - lactoglobulin, and “would not suggest that expression of non-native milk proteins, such as immunoglobulin fused to a non-milk enzyme ... would be successfully expressed at high levels.” As the examiner points out (Answer, page 17), Hyttinen provides an “example[,] which demonstrates that a non-milk protein, hEPO, is ... secreted at concentrations of greater than 0.1 mg/ml in transgenic milk (Hyttinen et al., see examples 1 and 3).” In addition, we find that Hyttinen disclose (e.g., column 3, lines 15-35), a process comprising the steps of creating a mammary gland specific expression system comprising regulatory elements needed for high level mammary gland specific expression derived from a milk protein gene or a mammary tumor virus, a DNA sequence encoding signal sequence needed for secretion and maturation of the fusion protein, a recombinant DNA encoding a

fragment or intact milk or non-milk protein, optionally a linker DNA sequence, and a recombinant DNA encoding said biologically active polypeptide.




We find no evidence on this record to suggest that a person of ordinary skill in the art at the time the invention was made would have had less than a reasonable expectation of success in placing the fusion construct taught by Rybak into the expression construct of Hyttinen to produce the fusion protein in milk at a concentration of at least 0.1 mg/ml. Accordingly, we are not persuaded by appellants' unsupported assertion of unexpected results.

CONCLUSION

For the foregoing reasons, we are not persuaded by appellants' arguments of record. Accordingly, we affirm the rejection of claim 16 under 35 U.S.C. § 103 as being unpatentable over Hyttinen in view of Rybak. As set forth above, claims 1-8, 10-14, and 17-35 fall together with claim 16.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

)	
Joan Ellis)	
Administrative Patent Judge)	
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Donald E. Adams)	
Administrative Patent Judge)	APPEALS AND
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Eric Grimes)	
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